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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,562	12/05/2001	Daniel R. Salomon	302018.3003-100	2653

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,562	SALOMON ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the c ver she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF IDS AND STATUS OF THE CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 5/17/02 are acknowledged, entered and considered. Claims 1-36 are present for examination.

DISCLOSURE OBJECTED TO, MINOR INFORMALITIES

2. The disclosure is objected to because of the following informalities: on page 22, line 7, in the recitation "patents". It is believed to be typographical error. Appropriate correction is required.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7, 13, 19 and 28 are indefinite in the recitation "2-clorodeoxyadenosine". The term "2-clorodeoxyadenosine" is misspelled. The correct spelling is "chlorodeoxyadenosine". See e.g. claims 2, 8-12, 14, 20-26, 29-30 and 35 and Summary of the Invention in the instant specification. It is believed to be typographical error. Appropriate correction is required.

Claims 1-12 are substantially duplicates of claims 13-24 because independent claim 1 is directed to a method of ameliorating chronic allograft rejection in a human or animal allograft recipient by administering to the recipient in need of such treatment, in

combination, a therapeutically effective amount of cyclosporin and a therapeutically effective amount 2-CDA. Similarly, independent claim 13 is directed to a method of ameliorating chronic allograft rejection in a human or animal allograft recipient by administering to an allograft recipient a therapeutically effective amount of cyclosporin and a therapeutically effective amount 2-CDA. Although, claim 1 recites administering to the recipient in need of such treatment, but the preambles of claims 1 and 13 clearly state "A method of ameliorating chronic allograft rejection in a human or animal allograft recipient". Thus, based on the preamble of claim 1, the phrase "in need of such treatment" is intended to allograft recipient. Further, claim 1 recites administering in combination of cyclosporin and 2-CDA, but claim 13 recites administering cyclosporin and 2-CDA. Thus, without reciting the term "in combination" one of ordinary skill in the art would understand that in claim 13 the cyclosporin and 2-CDA are combined for administering to allograft recipient. As such, there would appear to be no difference in scope between claims 1 and 13. Hence, both sets of claims appear to claim the same subject matter (See e.g., MPEP 706.03[k]).

CLAIMS REJECTION-35 U.S.C. § 102(b)

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 13, 25, 30-32, 35 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Nawrocki et al. (Transplantation Proceedings, Vol. 28, No. 6, pp. 3538-35-39, 1996).

The reference of Nawrocki et al. like the instantly claimed invention of claims 1, 13, 25, 30-32, 35 and 36 discloses a method and composition thereof for ameliorating or preventing chronic allograft rejection in a mammal by administering a therapeutically effective amount of cyclosporin and 2-chlorodeoxyadenosine (2-CDA), wherein said composition is administered subcutaneously and is efficient to suppress the recipient's B-cell mediated response to the allograft. The reference also discloses a prolongation of cardiac allograft survival in rats (mammals) following combination treatment with 2-CDA and cyclosporin resulting in efficient inhibition of B-cell function including activation, differentiation, and immunolglobulin production, and as such, substantially discloses the claimed invention (See e.g., pages 3538 and 3539 and Table I). Thus, in the absence of evidence to the contrary, the claimed method and composition for ameliorating or preventing chronic allograft rejection by administering therapeutically effective amount of cyclosporin and 2-CDA disclosed by the reference anticipates claims 1, 13, 25, 30-32, 35 and 36 as drafted.

5. Claims 1, 3, 13, 25, 27 and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Schmid et al. (Eur. Surg. Res., Vol. 30, pp. 61-68, 1998).

The reference of Schmid et al. like the instantly claimed invention of claims 1, 3, 13, 25, 27, and 30-32 discloses a method and composition thereof for ameliorating or preventing chronic allograft rejection in a mammal by administering a therapeutically effective amount of cyclosporin and 2-CDA (See e.g., pages 61-63 and 66-67) as directed to claims 1, 13, 25 and 30-32. The composition is administered orally and the

cyclosporin is provided at 10 mg/kg body weight which overlaps with the claimed ranges of claims 3 and 27 (See e.g., page 61). Thus, in the absence of evidence to the contrary, the claimed method and composition for ameliorating or preventing chronic allograft rejection by administering therapeutically effective amount of cyclosporin and 2-CDA disclosed by the reference anticipates claims 1, 3, 13, 25, 27 and 30-32 as drafted.

6. Claims 1, 3, 13, 25, 27, 28 and 31-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Cramer et al. (Transplantation Proceedings, Vol. 29, page 616, 1997).

The reference of Cramer et al. like the instantly claimed invention of claims 1, 3, 13, 25, 27, 28 and 31-36 discloses a method and composition thereof for ameliorating or preventing chronic allograft rejection including arterial atherosclerosis in a mammal by administering a therapeutically effective amount of cyclosporin and 2-chlorodeoxyadenosine (2-CDA), wherein the cyclosporin is provided at 5 mg/kg body weight and 2-CDA at 1 mg/kg body weight which overlaps with the claimed ranges of claims 3, 27 and 28. The composition is efficient to suppress the recipient's B-cell mediated response to the allograft. Thus the reference discloses the use of 2-CDA in combination with cyclosporin to inhibit or prevent the development of transplant arterial atherosclerosis in rats (mammals) cardiac allograft, and as such, substantially discloses the claimed invention (See e.g., page 616 and Table I). Therefore, in the absence of evidence to the contrary, the claimed method and composition for ameliorating or preventing chronic allograft rejection including arterial atherosclerosis by administering therapeutically effective amount of cyclosporin and 2-CDA disclosed by the reference anticipates claims 1, 3, 13, 25, 27, 28 and 31-36 as drafted.

CLAIMS REJECTION-35 U.S.C. § 103(a)

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nawrocki et al. (Transplantation Proceedings, Vol. 28, No. 6, pp. 3538-3539, 1996) taken with Schmid et al. (Eur. Surg. Res., Vol. 30, pp-61-68, 1998) and Cramer et al. (Transplantation Proceedings, Vol. 29, page 616, 1997).

The reference of Nawrocki et al. as discussed above discloses like the instantly claimed invention of claims 1, 13, 25, 30-32, 35 and 36 a method and composition thereof for ameliorating or preventing chronic allograft rejection in a mammal by

administering a therapeutically effective amount of cyclosporin and 2-chlorodeoxyadenosine (2-CDA), wherein said composition is administered subcutaneously and is efficient to suppress the recipient's B-cell mediated response to the allograft. The reference also discloses a prolongation of cardiac allograft survival in rats (mammals) following combination treatment with 2-CDA and cyclosporin resulting in efficient inhibition of B-cell function including activation, differentiation, and immunolglobulin production as directed to claims 1, 13, 25, 30-32 and 36 (See e.g., pages 3538 and 3539 and Table I).

The reference of Nawrocki et al. differs from claims 1-36 in not teaching the administration of specific dosages and duration time of cyclosporin and 2-CDA and preventing arterial atherosclerosis. However, the secondary reference of Cramer et al. discloses a method and composition thereof for ameliorating or preventing chronic allograft rejection including arteriosclerosis in a mammal by administering a therapeutically effective amount of cyclosporin and 2-chlorodeoxyadenosine (2-CDA), wherein the cyclosporin is provided at 5 mg/kg body weight and 2-CDA at 1 mg/kg body weight which overlaps with the claimed ranges of claims 3, 27 and 28. Further, the secondary reference of Schmid et al. discloses a method and composition thereof for ameliorating or preventing chronic allograft rejection in a mammal by administering a therapeutically effective amount of cyclosporin and 2-CDA (See e.g., pages 61-63 and 66-67) as directed to claims 1, 13, 25 and 30-32. The composition is administered orally and the cyclosporin is provided at 10 mg/kg body weight, which overlaps with the claimed ranges of claims 3 and 27 (See e.g., page 61). Furthermore, optimization of

dosages and duration of the dosages is within the purview of one of ordinary skill in the art and as admittedly acknowledged on pages 9 and 10 in the instant specification, the selected dosage level depend upon the activity of the particular compound, the route of administration, the severity of the condition being treated, and the condition and prior medical history of the patient being treated. However, it is within the skill of the art to start doses the compound at levels lower than required to achieve the desired therapeutic effect and to gradually increase the dosage until the desired effect is achieved. Thus, given the teachings of the secondary references and further as acknowledged on page 22, lines 1-2 in the instant disclosure, one skilled in the art will be able to readily adjust the 2-CDA dosage and duration time relation to a human patient's cyclosporin dosage and duration time to obtain the desired therapeutic effect.

Therefore, in view of the above, the combined teachings of the prior art makes obvious a method of ameliorating or preventing chronic allograft rejection including arterial atherosclerosis by administering effective amount of cyclosporin in combination with 2-CDA and a pharmaceutical formulation for administration thereof, absence of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDANCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

AM Mohamed/AAM

January 23, 2004